III. Targeted Testing and Treatment of Latent Tuberculosis Infection (LTBI)

A. The following individuals have a relatively high risk for progressing to TB disease and therefore should be given high priority for treatment for LTBI **regardless of age:**

TST≥ 0mm	TST≥ 5mm	TST≥ 10mm	TST≥ 15mm	Positive IGRA
HIV-positive or other severely immuno-compromised individuals (e.g. solid organ or bone marrow transplant) who are recent contacts to known or suspected infectious TB disease, regardless of previous treatment of LTBI HIV-positive with fibrotic changes on CXR consistent with prior TB who have received inadequate or no treatment for TB disease Children < 5 years of age identified as a recent contact to known or suspected infectious TB disease	HIV-positive Contacts to known or suspected infectious TB disease identified within the past two years Those with fibrotic changes on CXR consistent with prior TB and have received inadequate or no treatment for TB disease Immunocompromised individuals, e.g., receiving ≥ 15 mg per day of Prednisone for 1 mo., other immunosuppressive drugs, organ transplant, or persons taking or considering taking tumor necrosis factor (TNF) inhibitors like etanercept (Embrel ®), infliximab (Remicade ®) or anakinra (Kineret™) or adalimumab (Humira ®)	Foreign-born individuals from Asia, Africa, Caribbean, Latin America, Mexico, South America, Pacific Islands or Eastern Europe *Low prevalence countries are USA, Canada, Japan, Australia, Western Europe, and New Zealand* Those who have converted their TST within two years Those with medical conditions which place them at high risk for TB disease • diabetes mellitus • chronic renal failure • chronic malabsorption syndrome • leukemia, lymphomas, Hodgkin's disease • cancer of the head or neck • silicosis • weight loss of ≥ 10% ideal body weight • gastrectomy or intestinal bypass Injection drug or crack cocaine user Children < 4 years of age Children and adolescents exposed to high risk adults Persons staying for > 1 month with someone in a high incidence area Mycobacteriology lab personnel **The following individuals are at a lower risk for developing TB disease and are candidates for TLTBI if local resources are sufficient and the benefits outweigh the risk:** o Residents of long-term care facilities, and homeless shelters o Inmates in the DOC o Personnel in the following settings: • Prisons • Jails • Long-term care facilities • Hospitals and other health care facilities • Adult day care centers for HIV positive/AIDS • Homeless shelters	Persons with no risk factors for TB	Persons with a positive interferon gamma release assay (IGRA) regardless of risk factors/exposures should also be considered at risk to develop active TB disease, and should offered LTBI treatment.

B. Targeted testing identifies individuals at high-risk for developing TB who would benefit from treatment of LTBI. Decisions to treat LTBI should take into consideration the individual's risk for developing tuberculosis disease compared with the risk of adverse reactions to TB medication. Treatment of LTBI presumably acts by diminishing the bacterial population in healed or radiographically invisible lesions.

C. Standards for Managing Latent TB Infection

1. Prior to initiating any treatment for LTBI, review all medications the individual is taking and assess for potential drug interactions with TB medications.

2. All persons with LTBI should be offered HIV testing, regardless of perceived risk for HIV infection.

3. A review for symptoms of disease and a chest x-ray to exclude active tuberculosis disease are required before starting any treatment for latent infection:
   - A chest x-ray taken within the past two years is acceptable for asymptomatic HIV negative individuals with a remote positive PPD; and
   - A chest x-ray taken within the past three months is required for asymptomatic new converters, HIV+ individuals, and those who are severely immunocompromised.

4. If the patient reports a cough and sputum results are pending, wait until sputum culture results are reported as negative before starting medications.

5. Obtain a medical history including previous adverse reactions to TB drugs (e.g., drug fever, rash), underlying liver disease and INH-associated liver injury and offer HIV testing (**see TB Epidemiological Record – DHHS 1030).**

5. TB medications in institutional/congregate settings should be administered daily by direct observation.

6. For self-administration, never give more than a 30-day supply of INH or RIF.

7. Directly Observed Preventive Therapy (DOPT) must be used with all regimens administered once or twice weekly. DOPT is strongly recommended for:
   - Those with HIV infection;
   - Children < 5 years of age; and
   - Infected close contacts to isoniazid (INH) or rifampin (RIF) resistant TB.

8. Certain TB drugs should be calculated according to mg/kg body weight. Calculate on the lower figure in the range and round up to the next available dose supplied by the manufacturer **(see Chapter IV for dosage table).**

9. The health care provider or an interpreter should be conversant in the patient's own language to ensure good communication.

10. *All patients should be instructed to stop their medication and seek immediate medical consultation if they experience loss of appetite, abdominal pain, nausea, vomiting, jaundice or other symptoms of hepatitis.*

11. All patients must be clinically assessed at least monthly for adverse reactions and the findings documented **(see TB Flow Sheet – DHHS 2810).**

12 The appropriate drug information fact sheet(s) should be reviewed with the patient.

13 Health department TB nurses may manage latent TB infection under standing orders signed by a physician or contract TB clinician. **(see Chapter III, section K. for an example of standing orders.)**

D. Standard Regimens for HIV Negative Adults ≥ 15 Years

1. INH for nine months
   - Nine months of INH offers a high degree of protection against the progression of TB infection to TB disease (approximately 90 percent in individuals who complete a full course of therapy).
   - Dosage for INH is 5 mg/kg (maximum 300mg) daily (270doses) or 15mg/kg (maximum 900mg) twice-weekly DOPT (78 doses) for a total of nine months to be taken within a 12-month period of time.
   - INH for LTBI is relatively contraindicated for individuals with active hepatitis or end-stage liver disease and should not be used in these individuals without a specific physician order.

2. INH for six months:
   - Six-month regimen of INH offers an acceptable degree of protection against the progression of TB infection to TB disease (approximately 70 percent in individuals who complete a full course of therapy)
   - Dosage for INH is 300 mg daily (180 doses) or 900 mg twice-weekly DOPT (52 doses) for a total of 6 months to be taken within a nine-month period of time.
   - Six months of INH will be considered an adequate course of treatment for LTBI when nine months cannot be completed.
   - INH for LTBI is relatively contraindicated for individuals with active hepatitis or end-stage liver disease and should not be used in these individuals without a specific physician order.

3. RIF for four months:
   - This regimen is an acceptable alternative to INH and would be preferred in the following circumstances:
     - Intolerance to INH;
     - Individual is a close contact to INH-resistant, RIF-susceptible TB;
     - Individual is high-risk for progression to active TB but is unlikely to adhere to a full nine-month course of INH; and
     - Individual is at relatively high risk for hepatotoxicity from INH (e.g. excess alcohol use, concurrent hepatotoxic medication).
   - RIF interacts with many other medications, including oral contraceptives and warfarin. **The patient's medication regimen should be carefully examined for potential medication interactions before prescribing RIF**.
   - Dosage for RIF is calculated according to body weight and rounded up to the next available dose. 10 mg/kg per day with a daily maximum of 600 mg.
   - Daily RIF (120 doses) should be given for a total of four months within a six-month period of time
   - **RIF by itself may not be given on a twice-weekly schedule**.

4. Three months of isoniazid-rifapentine (12 doses)

- Isoniazid plus rifapentine, administered once-weekly by directly observed therapy for 12 weeks, is an option for some individuals with latent TB infection, particularly persons unlikely to complete a longer treatment regimen.
- Isoniazid is administered at a dose of 15 mg/kg (maximum 900 mg), plus 15 mg/kg of rifapentine (maximum 900 mg), given together once weekly for 12 weeks, taken within a 16 week period of time. Missed doses can still be administered up to 72 hours before the next dose.
- Regimen is contraindicated for pregnant and breastfeeding women.
- Regimen is contraindicated in HIV-positive individuals who are on highly-active antiretroviral therapy (HAART). However, it can be safely used in most individuals who are not on HAART.
- Rifapentine interacts with many other drugs. Please see Chapter VI of the NC TB Control Manual for a *partial* list of drugs that interact with rifapentine.
- Health department nurses must enter all patients using this regimen into the North Carolina Disease Surveillance System (NCEDSS). The contact or LTBI wizard must be completed, including treatment completion information.
- Note that 11 doses taken within 16 weeks is adequate for completion of INH/rifapentine treatment

5. RIF-PZA
   - RIF-PZA for treatment of latent TB infection is **no longer recommended** for routine use due to the unacceptable incidence of severe hepatitis resulting in hospitalization, liver transplantation and sometimes death. Only when a strict clinical protocol is being followed under the direction of a physician and has been approved by the NC TB Control Program Medical Director should this regimen be undertaken.
   - **RIF and PZA remain essential elements in the standard regimen for treating active TB disease.**

E. Standard Adult Regimens for Inadequately or Untreated Previous TB

1. Individuals with a chest x-ray suggestive of fibrotic lesions thought to represent previous TB and positive Interferon Gamma Release Assay (IGRA) or TST (≥ 5mm) should be treated for LTBI after active TB disease has been ruled out. Treatment options are:
   - INH for nine months; or
   - RIF (with or without INH) for four months **RIF by itself must be taken daily.**
   - INH plus rifapentine once-weekly for 12 weeks

2. Individuals with chest x-rays suggestive of healed primary TB disease (i.e. calcified solitary pulmonary nodules, calcified hilar lymph nodes, and apical pleural scarring) and positive IGRA or TST (≥ 5mm) are not at increased risk for TB disease. The need for treating LTBI in healed primary TB disease should be determined by:
   - Size of the TST; and
   - Risk factors for progression to disease.

F. Standard Regimens for HIV-Negative Infants and Children (< 15 Years)

1. Nine months of INH
   - Dosage for INH is calculated according to body weight and rounded up to the next available dose. Dosage is 10 mg/kg for daily dose (maximum 300 mg) and 20 mg/kg (maximum 900 mg) for twice weekly dose.
   - Daily INH (270 doses) or twice-weekly DOPT (78 doses) should be given for a total of nine months within a 12-month period of time.

2. Four months of RIF (120 doses).
   - This regimen would be preferred in the following circumstances:
     - Intolerance to INH;
     - Individual is a close contact to INH-resistant, RIF-susceptible TB;
     - Individual is high-risk for progression to active TB but is unlikely to adhere to a full nine-month course of INH; and
     - Individual is at relatively high risk for hepatotoxicity from INH (e.g. excess alcohol use, concurrent hepatotoxic medication).
   - Dosage for RIF is 10-20 mg/kg, rounding up to the next available dose, daily (120 doses) for a total of 4 months taken within a six month period of time
   - **RIF by itself may not be given on a twice-weekly schedule.**
   - RIF interacts with many other medications, including oral contraceptives and warfarin. The patient's medication regimen should be carefully examined for potential medication interactions before prescribing RIF.
   - Children weighing more than 40 kg should be dosed as an adult

3. Three months of isoniazid-rifapentine (12 doses)
   - Can be given to children over two years of age.
   - Isoniazid plus rifapentine, administered once-weekly by directly observed therapy for 12 weeks, is an option for some individuals with latent TB infection, particularly persons unlikely to complete a longer treatment regimen.
   - Isoniazid is administered at a dose of 20 mg/kg (maximum 900 mg), plus 20 mg/kg of rifapentine (maximum 900 mg), both rounding up to the next available dose, given together once weekly for 12 weeks, taken within a 16 week period of time.
   - Children weighing more than 40 kg should be dosed as an adult.
   - Missed doses can still be administered up to 72 hours before the next dose.
   - Regimen is contraindicated in HIV-positive individuals who are on highly-active antiretroviral therapy (HAART). However, it can be safely used in most individuals who are not on HAART.
   - Rifapentine interacts with many other drugs. Please see Chapter VI of the NC TB Control Manual for a *partial* list of drugs that interact with rifapentine.
   - Health department nurses must enter all patients using this regimen into the North Carolina Disease Surveillance System (NCEDSS). The contact or LTBI wizard must be completed, including treatment completion information.
   - Note that 11 doses taken within 16 weeks is adequate for completion of INH/Rifapentine treatment.

Weigh child at least monthly and adjust dosage as weight changes

G. Standard Regimen for HIV-Negative Pregnant Women

1. Chest x-rays

- Due to the risk of progressive and/or congenital TB, pregnant women should have a PA view of the chest (with appropriate shielding) as soon as possible, even during the first trimester of pregnancy, if they have a positive TST or IGRA.

2. Asymptomatic TST/IGRA positive pregnant women with a negative chest x-ray should start latent tuberculosis treatment as soon as possible if they have one of the following factors:
   - HIV infection;
   - Close contact to infectious TB disease;
   - TST/IGRA conversion; or
   - Medical condition associated with high risk of progression to active TB disease.

3. Asymptomatic TST/IGRA positive pregnant women with a negative chest x-ray and no risk factors may elect to delay preventive therapy until after delivery, but it is acceptable to offer preventive therapy with INH or RIF during pregnancy with appropriate monitoring.

4. Treatment Regimens

   a. INH for nine months:
      - Dosage for INH is 300mg daily (270 doses) or 900mg twice-weekly DOPT (78 doses) for a total of nine months to be taken within a 12 month period of time;
      - Six months of INH given within a 9 month period of time will be considered an adequate course of treatment for LTBI when nine months cannot be completed; and
      - INH for LTBI is relatively contraindicated for individuals with active hepatitis or end-stage liver disease.

   b. RIF for four months is an acceptable alternative for pregnant women This regimen would be preferred in the following circumstances:
      - Intolerance to INH;
      - Individual is a close contact to INH-resistant, RIF-susceptible TB;
      - Individual is high-risk for progression to active TB but is unlikely to adhere to a full nine-month course of INH; and
      - Individual is at relatively high risk for hepatotoxicity from INH (e.g. excess alcohol use, concurrent hepatotoxic medication).
      - RIF interacts with many other medications, including oral contraceptives and warfarin. The patient's medication regimen should be carefully examined for potential medication interactions before prescribing RIF.
      - Dosage for RIF is calculated according to body weight and rounded up to the next available dose. 10 mg/kg per day with a daily maximum of 600 mg.
      - Daily RIF (120 doses) should be given for a total of four months within a six-month period of time.
      - **RIF by itself may not be given on a twice-weekly schedule.**

5. The small concentration of TB medication in breast milk does not produce toxicity in the newborn; therefore breast-feeding should not be discouraged.

H. Pyridoxine

1. Peripheral neuropathy is associated with the use of INH but is uncommon at doses of 5 mg/kg of body weight.

2. Pyridoxine (B_6) 25 mg. daily or 50 mg. twice weekly (once weekly with INH/rifapentine) should be given on the same schedule with INH if the following risk factors for peripheral neuropathy are present:
   a. Diabetes mellitus;
   b. Average alcohol use of > three drinks per day or binge drinking (≥ five drinks in one day intermittently);
   c. Malnutrition;
   d. HIV infection;
   e. Pregnancy, if prenatal vitamin does not contain at least 25 mg of B_6; and
   f. Seizure disorder.

3. Individuals who develop peripheral neuropathy while taking daily B_6 should have their B_6 dose doubled. If neuropathy is not resolved in two weeks, consult physician.

4. Individuals on dialysis should be given B_6 50mg on the same schedule with INH.

5. Pyridoxine (B_6) is recommended for exclusively breastfed infants and for children and adolescents on meat and milk deficient diets; children with nutritional deficiencies, including all symptomatic HIV-infected children.

   a. Dosage for infants and children (contact physician for order):
      - 1 mg/kg body weight (maximum 25mg daily); dose can be rounded up as needed. For example, a 14 lb. infant weighs 6.36 kg and therefore would receive 6.36 mg of pyridoxine. Using a graduated syringe or dropper, 6.4 mg would be acceptable.

   b. Frequency:
      - Daily.

   c. Preparation:
      - pharmacist should prepare 99 cc of simple sugar syrup and add one vial (100 mg) of injectable pyridoxine. This preparation results in a concentration of 1mg of pyridoxine per cc of syrup.

   d. Administration:
      - By mouth, using a pediatric oral syringe or dropper; the syringe or dropper should be graduated in 0.1 - 0.2 cc to allow for correct dosing.

   e. Storage:
      - Syrup should be placed in an amber glass bottle and stored in the refrigerator. The syrup is stable for 30 days.

   f. Alternatively, pyridoxine tablets (25 mg) may be quartered (6.25 mg), crushed, and mixed with baby food or breast milk for administration.

I. Monitoring of LTBI

1. INH monitoring

a. Prior to initiating INH, obtain a baseline hepatic function panel[1] (includes: aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, and total bilirubin) on the following individuals:

- Average alcohol use of ≥three drinks per day or binge drinking (≥five drinks in one day, intermittently) (one drink is defined as one 12 oz beer, 4 oz of wine or 1 oz of liquor).
- HIV-positive.
- Underlying liver disease.
- Pregnant women.
- Women up to three months postpartum.
- Those currently taking other potentially hepatotoxic drugs such as:[1]
  - ♦ "statin" drugs;
    - atorvastatin (Lipitor)
    - cerivastatin (Baycol)
    - lovastatin (Mevacor)
    - pravastatin (Pravachol)
    - rosuvastatin (Crestor)
    - simvastatin (Zocor)
  - ♦ anticonvulsant drugs;
    - carbamazepine (Tegretol)
    - phenytoin (Dilantin)
    - valproic acid (Depakote)
  - ♦ methotrexate; and
  - ♦ miscellaneous antidiabetic agents for Type 2 diabetes.
    - pioglitazone (Actos)
    - rosiglitazone (Avandia)

If baseline lab tests are abnormal consult the physician before initiating treatment for LTBI.

b. Obtain hepatic function panel[2] monthly on the following individuals who are taking INH:

- Baseline hepatic function panel results are abnormal;
- Pregnant women;
- Women up to three months postpartum the immediate postpartum period (i.e., within three months of delivery);
- Those with symptoms of adverse reactions;
- Taking potentially hepatotoxic drugs (above list);
- Those with chronic active hepatitis B or those with hepatitis C;
- Chronic or binge use of alcohol; and
- Those with HIV infection.

Hold therapy if signs or symptoms of hepatotoxicity are present, draw hepatic function panel and consult physician with results.

[1] Note that this is an incomplete list of drugs with potential for hepatotoxicity

[2] Hepatic Function Panel includes: aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, and total bilirubin.

c. See the last pages of this chapter for a flowchart on how to address hepatotoxicity in patients taking TB medications.

d. Complete CDC National Surveillance for Severe Adverse Event data collection form in chapter IX if the patient has hepatotoxicity severe enough to require hospitalization or death and send to regional nurse consultant.

2. RIF monitoring

a. Prior to initiating RIF, obtain a baseline CBC with platelets, and hepatic function panel[1] on the following individuals:

- average alcohol use of ≥ three drinks per day or binge drinking (≥ five drinks in one day, intermittently) (one drink is defined as one 12 oz beer, 4 oz of wine or 1 oz of liquor).
- HIV positive.
- Underlying liver disease.
- Pregnant women.
- Those currently taking other potentially hepatotoxic drugs such as:[1]
  - ♦ "statin" drugs;
    - atorvastatin (Lipitor)
    - cerivastatin (Baycol)
    - lovastatin (Mevacor)
    - pravastatin (Pravachol)
    - rosuvastatin (Crestor)
    - simvastatin (Zocor)
  - ♦ anticonvulsant drugs;
    - carbamazepine (Tegretol)
    - phenytoin (Dilantin)
    - valproic acid (Depakote)
  - ♦ methotrexate; and
  - ♦ miscellaneous antidiabetic agents for Type 2 diabetes.
    - pioglitazone (Actos)
    - rosiglitazone (Avandia)

b. If baseline CBC with platelets and liver function panel are outside normal limits, consult physician before initiating treatment for LTBI.

c. Obtain hepatic function panel[2] monthly on the following individuals who are taking RIF only:

- Baseline hepatic function panel results are abnormal;
- Pregnant women;
- Women up to three months postpartum the immediate postpartum period (i.e., within three months of delivery);
- Those with symptoms of adverse reactions;
- Persons taking potentially hepatotoxic drugs (above list);
- Persons with chronic active hepatitis B or those with hepatitis C;
- Chronic or binge use of alcohol; and
- Those with HIV infection.

[1] Note that this is an incomplete list of medications with potential for hepatotoxicity
[2] Hepatic Function Panel includes: aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, and total bilirubin.

Hold therapy if <u>signs or symptoms</u> of hepatotoxicity are present; draw hepatic function panel and consult physician. RIF can also cause immunologic reactions, including fevers, anemia, and thrombocytopenia. Hold therapy for any new fevers or easy bruising/bleeding.

3. Isoniazid/rifapentine monitoring

a. Prior to initiating INH/rifapentine, obtain a baseline hepatic function panel[1] (includes: aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, and total bilirubin) and complete blood count (CBC) with platelets on the following individuals:

- Average alcohol use of ≥ three drinks per day or binge drinking (≥ five drinks in one day, intermittently) (one drink is defined as one 12 oz beer, 4 oz of wine or 1 oz of liquor).
- HIV-positive.
- Underlying liver disease.
- Women up to three months postpartum.
- Those currently taking other potentially hepatotoxic drugs such as:[1]
  - ♦ "statin" drugs;
    - atorvastatin (Lipitor)
    - cerivastatin (Baycol)
    - lovastatin (Mevacor)
    - pravastatin (Pravachol)
    - rosuvastatin (Crestor)
    - simvastatin (Zocor)
  - ♦ anticonvulsant drugs;
    - carbamazepine (Tegretol)
    - phenytoin (Dilantin)
    - valproic acid (Depakote)
  - ♦ methotrexate; and
  - ♦ miscellaneous antidiabetic agents for Type 2 diabetes.
    - pioglitazone (Actos)
    - rosiglitazone (Avandia)

If baseline lab tests are abnormal consult the physician before initiating treatment for LTBI.

b. Individuals on INH/RPT should be monitored clinically at least once per month while on medications. At each visit, patients should be questioned and examined for the following:

- Signs or symptoms of hepatotoxicity (e.g., anorexia, nausea, vomiting, abdominal pain, jaundice);
- Signs or symptoms of hypersensitivity (fever, chills, myalgias; and)
- Signs or symptoms of thrombocytopenia (easy bruising or bleeding, petechiae, purpura).

Hold therapy if signs or symptoms of hepatotoxicity, hypersensitivity, and/or thrombocytopenia are present.

c. Obtain hepatic function panel[1] monthly on the following individuals who are taking INH/RPT:

[1] Note that this is an incomplete list of drugs with potential for hepatotoxicity

- Baseline hepatic function panel results are abnormal;
- Pregnant women;
- Women up to 3 months postpartum the immediate postpartum period (i.e., within 3 months of delivery);
- Those with symptoms of adverse reactions;
- Persons taking potentially hepatotoxic drugs (above list);
- Persons with chronic active hepatitis B or those with hepatitis C;
- Chronic or binge use of alcohol; and
- Those with HIV infection.

d. See the last few pages of this chapter for a flowchart on how to address hepatotoxicity in patients taking TB medications.

e. Complete CDC National Surveillance for Severe Adverse Event data collection form (chapter IX, pages 67-71) if the patient has hepatotoxicity severe enough to require hospitalization or death and send to regional nurse consultant.

J. Closure of Patient Record for Non-Adherence

a. Contact patient by telephone within 14 days of failure to pick up medication.
b. If unable to reach by phone or no response to call, send a letter identifying the benefits of TLTBI and symptoms of tuberculosis disease; advise patient to contact you within two weeks (give date) or record will be closed.
c. If no response to letter or patient refuses treatment, close patient's record to follow-up.

[1] Hepatic Function Panel includes: aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, and total bilirubin.

K. Standing Orders Examples

Intended as an example for required components only, not as best practice- all standing orders should reflect individual agency protocols determined by the Medical Director.

Standing Order: Evaluation and Treatment of Latent TB Infection Using Rifampin

All RNs employed or contracted by the agency who have completed orientation will use standing orders for the evaluation and treatment of latent TB infection using rifampin.

Assessment:

1. **Objective findings:**
   - The tuberculin skin test is positive (based on guidance from the NC TB Control Manual), or an interferon gamma release assay for TB is positive.
   - No sputum culture pending.
   - Chest x-ray interpretation indicating no evidence of active TB disease. The chest x-ray must have been taken within the past two years for asymptomatic HIV negative individuals with a remote positive PPD. A chest x-ray taken within the past three months is required for asymptomatic new converters, HIV positive individuals, and those who are severely immunocompromised.

2. **Subjective findings:**
   - History provided by the patient or medical record indicates:
     a. There are no symptoms of TB;
     b. No history of underlying liver disease, or previous reactions to rifampin; and
     c. Has not received adequate treatment for latent TB infection in the past.

Plan of Care:

1. **Implementation:**
   - Obtain posterior-anterior (PA) view chest x-ray.
   - Children under age five should also have a lateral view chest x-ray.
   - Complete a Tuberculosis Epidemiological Record (DHHS 1030).
   - Obtain HIV test unless the patient specifically refuses or has documentation of testing with the past 6 months.
   - For adults (≥ 15 years of age) over 45 kg: Initiate rifampin (RIF) 600 mg daily for four months. If less than 45 kg., initiate 10 mg/kg of body weight daily for four months, rounding up to the nearest 150 mg.
   - For children (< 15 years of age): Initiate rifampin (RIF) 10 mg/kg of body weight (maximum 600 mg) daily for four months, rounding up to the nearest 150 mg.
   - Adjust dosage as weight changes
   - If the patient is on a medication that will interact with rifampin, is allergic or intolerant of rifampin, or is a contact to a rifampin resistant case of tuberculosis, initiate INH using the "Evaluation and Treatment of Latent TB Infection Using INH standing orders

Nursing Action:

- Advise the patient of common adverse reactions to rifampin.
- Advise the patient to hold medications and contact the health department if adverse reactions such as, nausea and vomiting, loss of appetite, dark urine, jaundice, malaise, abdominal pain, tenderness or discomfort, skin rash, fever, anemia, thrombocytopenia (unexplained bruising/bleeding) occur.
- Ensure that physician reviews and signs all lab work results.

Criteria for calling the Physician:

For patients with the following conditions do **not** use standing orders. Instead call physician for specific treatment and monitoring orders. Recommendations for treatment and monitoring of these individuals can be found in chapter 3 of the NC TB Control Manual.

- History of hepatitis or liver disease.
- History of adverse reaction to rifampin
- Documented excess/binge alcohol use.
- Pregnant or up to 3 months postpartum.
- Exposed to drug resistant case of TB.
- On anticonvulsant drugs or any other potentially hepatotoxic drugs such as:
    - "Statin drugs
        - Atorvastatatin (Lipitor)
        - Cerivastatin (Baycol)
        - Lovastatin (Mevacor)
        - Pravastatin (Pravachol)
        - Rosuvastatin (Crestor)
        - Simvastatin (Zocor)
    - Pioglitazone (Actos), rosiglitazone (Avandia)
    - Acetaminophen (Tylenol)
    - Methotrexate
    - Sulfasalazine (Azulfidine)
    - Duloxetine (Cymbalta)

    This list is not exhaustive, and reports of hepatotoxicity related to other medications are frequently published, so the complete medication list should be reviewed by a physician or pharmacist prior to initiation of LTBI treatment.
- Taking other medication that may interact with rifampin (including warfarin, oral contraceptives, corticosteroids, immunosppressive medications such as cyclosporine, tacrolimus, HIV medications) **The patient's medication list should be reviewed with a physician or pharmacist to determine if a potential drug interaction exists.**
- Chest x-ray suggestive of previous TB.
- HIV positive or has other immunosuppressing conditions.
- On hemodialysis.
- Taking methotrexate.
- A child less than 5
- If baseline or follow-up lab work is abnormal.
- If patient complains of nausea and vomiting, loss of appetite, dark urine, jaundice, malaise, abdominal pain, tenderness or discomfort, skin rash, fever, anemia, thrombocytopenia (unexplained bruising/bleeding)while taking rifampin.

Follow-up Requirements:

- Evaluate the patient monthly using the Tuberculosis Flow Sheet (DHHS 2810).

Resources: NC TB Control Program Policy Manual

Legal Authority: Nurse Practice Act, G.S. 90-171.20 (7) (f) & (8) (c)

Date written:_____

Approved by: _____ Date:_____

Approved by: _____ Date:_____

Approved by: _____ Date:_____

Intended as an example for required components only, not as best practice- all standing orders should reflect individual agency protocols determined by the Medical Director.

Standing Order: Evaluation and Treatment of Latent TB Infection Using INH

All RNs employed or contracted by the agency who have completed orientation will use standing orders for the evaluation and treatment of latent TB infection using INH when rifampin cannot be used.

Assessment:

1. **Objective findings:**
   - The tuberculin skin test is positive (based on guidance from the NC TB Control Manual), or an interferon gamma release assay for TB is positive.
   - No sputum culture pending.
   - Chest x-ray interpretation indicating no evidence of active TB disease.
2. **Subjective findings:**
   - History provided by the patient or medical record indicates:
     a. There are no symptoms of TB;
     b. No history of underlying liver disease, or previous reactions to INH; and
     c. Has not received at least six months of treatment for latent TB infection in the past.
     d. Is not a contact to an INH resistant case of tuberculosis

Plan of Care:

Implementation:

- Obtain posterior-anterior (PA) view chest x-ray.
- Children under age five should also have a lateral view chest x-ray.
- Complete a Tuberculosis Epidemiological Record (DHHS 1030).
- Obtain HIV test.
- For adults (> 15 years of age): Initiate Isoniazid (INH) 5 mg/kg (maximum 300 mg) daily for nine months.
- For children (< 15 years of age): Initiate Isoniazid (INH) 10 mg/kg (maximum 300 mg) daily for nine months.
- Initiate Pyridoxine (B6) 25 mg per day along with INH if the patient is an adult and has any of the following conditions:
  a. Diabetes
  b. Alcohol use of > 3 drinks per day
  c. Malnutrition
  d. Seizure disorder

Nursing Action:

- Advise the patient of common adverse reactions to INH.
- If during the course of treatment for latent TB infection, the patient complains of nausea, vomiting, loss of appetite, dark (tea or cola colored) urine, malaise, abdominal tenderness or bloating, yellow skin or sclera, instruct the patient to hold medications, draw hepatic function panel, and call physician.
- Ensure that physician reviews and signs all lab work results.

Criteria for calling the Physician:

For patients with the following conditions do **not** use standing orders. Instead call physician for specific treatment and monitoring orders. Recommendations for treatment and monitoring of these individuals can be found in chapter 3 of the NC TB Control Manual.

- History of hepatitis or liver disease.
- History of adverse reaction to rifampin

- Documented excess/binge alcohol use.
- Pregnant or up to 3 months postpartum.
- Exposed to drug resistant case of TB.
- On anticonvulsant drugs or any other potentially hepatotoxic drugs such as:
    - "Statin drugs
        - Atorvastatatin (Lipitor)
        - Cerivastatin (Baycol)
        - Lovastatin (Mevacor)
        - Pravastatin (Pravachol)
        - Rosuvastatin (Crestor)
        - Simvastatin (Zocor)
    - Pioglitazone (Actos), rosiglitazone (Avandia)
    - Acetaminophen (Tylenol)
    - Methotrexate
    - Sulfasalazine (Azulfidine)
    - Duloxetine (Cymbalta)

      This list is not exhaustive, and reports of hepatotoxicity related to other medications are frequently published, so the complete medication list should be reviewed by a physician or pharmacist prior to initiation of LTBI treatment.
- Taking other medication that may interact with INH. **The patient's medication list should be reviewed with a physician or pharmacist to determine if a potential drug interaction exists**
- Chest x-ray suggestive of previous TB.
- HIV positive or has other immunosuppressing conditions.
- On hemodialysis.
- Taking methotrexate.
- If baseline or follow-up lab work is abnormal.
- If patient complains of nausea, vomiting, loss of appetite, dark (tea or cola colored) urine, malaise, abdominal tenderness or bloating, yellow skin or sclera while taking INH.

Follow-up Requirements:

- Evaluate the patient monthly using the Tuberculosis Flow Sheet (DHHS 2810).

Resources: NC TB Control Program Policy Manual

Legal Authority: Nurse Practice Act, G.S. 90-171.20 (7) (f) & (8) (c)

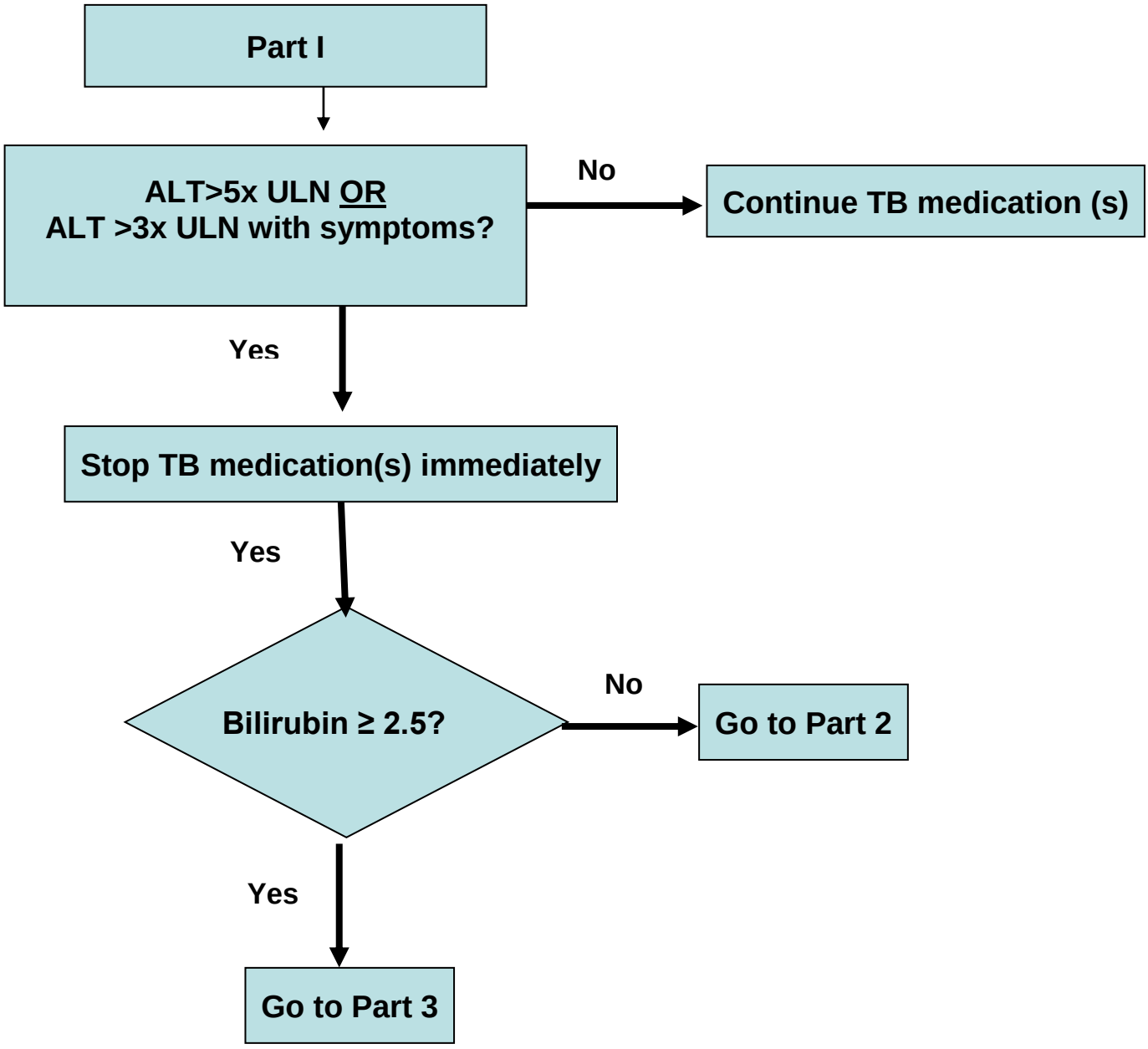
Date written:_____

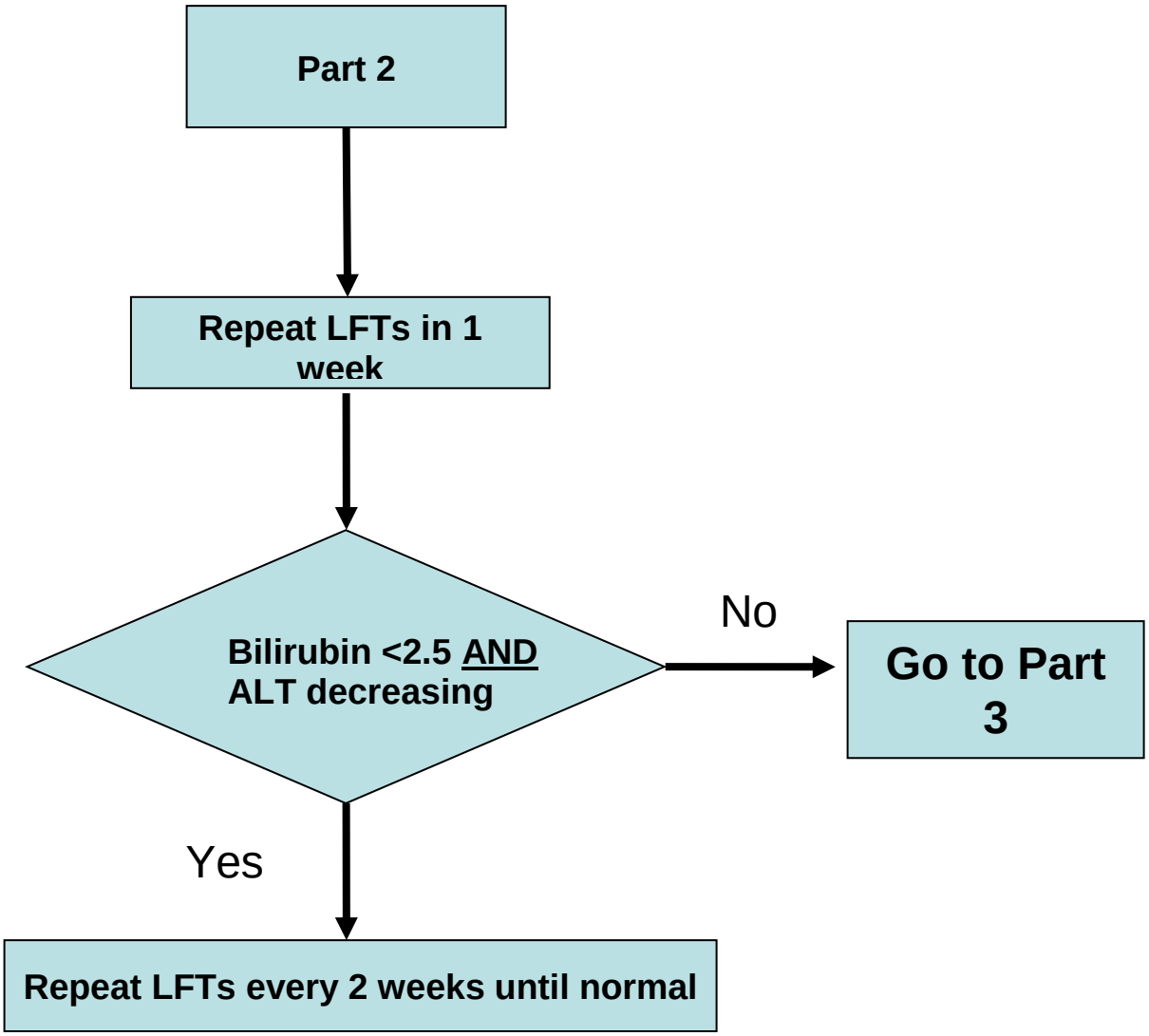
Approved by: _____ Date:_____

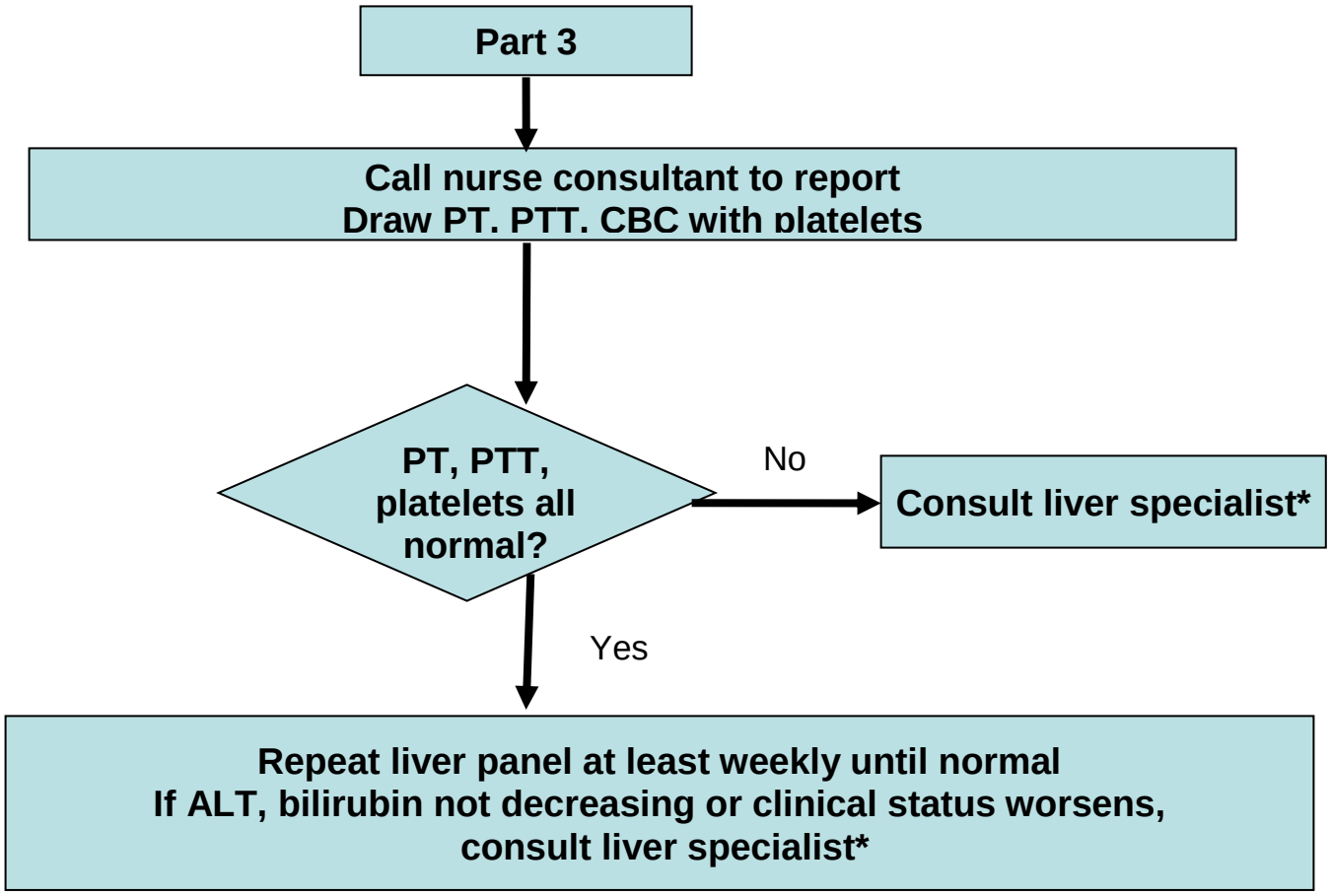
Approved by: _____ Date:_____

Approved by: _____ Date:_____

L. Hepatotoxicity Flowchart




Part 2
Repeat LFTs in 1 week
Bilirubin <2.5 AND ALT decreasing
No
Go to Part 3
Yes
Repeat LFTs every 2 weeks until normal



* The nurse consultant/state TB medical consultant can facilitate this referral—please contact immediately